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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,739	02/21/2002	Walter Callen	09010-107001 / DIVER1530-	1077
45975	7590	05/03/2006	EXAMINER	
DIVERSA C/O MOFO S.D. 12531 HIGH BLUFF DRIVE SUITE 100 SAN DIEGO, CA 92130-2040			RAO, MANJUNATH N	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/081,739

Applicant(s)

CALLEN ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 49-62, 68-75, 95-100, 107, 111-115 and 117-122 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 6, 12, 16, 29, 47, 48, 74, 75, 87, 88, 101-106 and 130-132 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 9-9-05
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

Continuation of Disposition of Claims: Claims pending in the application are 1,2,6,12,16,29,47-62,68-75,87,88,95-107,111-115,117-122 and 130-132.

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### **DETAILED ACTION**

Claims 1-2, 6, 12, 16, 29, 47-62, 68-75, 87-88, 95-107, 111-115, 117-122, 130-132 are currently pending and are present for examination. Claims 1-2, 6, 12, 16, 29, 47-48, 74-75, 87-88, 101-106, 130-132 are now under consideration. Claims 49-62, 68-73, 95-100, 107, 111-115, 117-122 remain withdrawn from consideration as being drawn to non-elected invention.

Applicants' amendments and arguments filed on 2-17-06, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. With respect to applicant's request to rejoin claims drawn to method of making and using, Examiner will do so when claims drawn to the products are in condition for allowance.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 47, 48, 130 and 132 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 47, 48, 130 is drawn to a method of producing a recombinant polypeptide by introducing the nucleic acid sequence of claim 1 or 2 into a host cell. However, the claim does not make it clear that said host cell is an isolated host cell and therefore when interpreted broadly, could read on a cell attached to a human being. Such a limitation could very well read on the transformation of a cell attached to a human being even though all the cells in a human being may not be transformed with said DNA. Claims that read on a human being are considered non-statutory subject matter. On similar lines claim 132 is

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drawn to "A host cell comprising the nucleic acid of claim 1, wherein ...said cell is a eukaryotic cell". Here again the claim does not make it clear that said host cell is an isolated host cell and therefore could be interpreted as still attached to a human being which is considered as non-statutory subject matter. Therefore claims 130 and 132 are rejected under 35 U.S.C. 101.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2 and claims 6, 12, 16, 29, 47-48, 74-75, 87-88, 101-106, 130-132 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 2 recite the phrase "sequences complementary to (a)". It is not clear to the Examiner whether applicant means that the sequences are full length complements or partial complement. In view of this ambiguity, Examiner has broadly considered the phrase to mean both, full length complements and partial length complement.

Claim 75 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 75 recites the limitation "the oligonucleotide" in line 1. There is insufficient antecedent basis for this limitation in the claim.

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Claims 2, 74-88 and claims 101-106 and 130-132 depending therefrom are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2 and 74 recite the phrase "0.15 NaCl". Said phrase makes no scientific sense. Applicants perhaps meant to recite "0.15 Molar NaCl". If that is so and if applicants can show support for said phrase, amending the claim accordingly would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 74-88 and claims 101-106 and 130-132 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 2 and 74 have been amended to recite the stringent hybridization conditions which comprises a hybridization in a buffer comprising 0.1X SSC, 0.5% SDS, 0.15 (Molar?) NaCl for 15 minutes at about 72 degree C and a wash step. However, a perusal of the specification indicates that applicants have no support for said stringent hybridization using said buffer. While Examiner found support for "hybridization under stringent conditions" on page 18 (paragraph 0071 and 0072) of the specification which comprises an entirely different buffer, he was unable to find support for the specific hybridization buffer and conditions recited in the claim. Therefore claims 2, 74-88 are

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rejected for introducing new matter into the claims. Examiner believes that applicants have misquoted the above buffer as hybridization buffer while actually the buffer is a wash buffer to be used in the washing step.

Claims 1-2, 6, 12, 16, 29, 47-48, 74-75, 87-88, 101-106, 130-132 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide with SEQ ID NO:1 encoding an enzyme with SEQ ID NO:2, or a polynucleotide that is at least 95% identical to SEQ ID NO:1 encoding a polypeptide having amylase activity, and polynucleotides that are full length complement thereof does not reasonably provide enablement for any such polynucleotide which are not full length complements of the above polynucleotides and probes wherein said probe hybridizes to amylase-encoding polynucleotide under highly stringent hybridization conditions claimed in claim 74, vectors, host cells comprising the above and method of making the polypeptides encoded by said polynucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-2, 6, 12, 16, 29, 47-48, 74-75, 87-88, 101-106, 130-132 are so broad as to encompass any polynucleotide comprising a polynucleotide that is either a full length

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complement or partially complement to the polynucleotide of claims 1 or 2 or any polynucleotide (probe) that simple hybridizes to the polynucleotides of claims 1 or 2 under the stringent wash conditions at 72 degree C.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single polynucleotide with SEQ D NO:1. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and polypeptides. The specification is limited to teaching the use of SEQ ID NO: 1 as that encoding an amylase but provides no guidance with regard to the making of and using of complements, probes or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.



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While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

On similar lines, claims directed to nucleic acid probes comprising oligonucleotides described above can hybridize to any polynucleotide encoding alpha amylase i.e., a variant or mutant of SEQ ID NO:1 irrespective of whether the polynucleotide comprising the same encodes a polypeptide with SEQ ID NO:2. The specification does not teach as to how those skilled in the art can use the same to detect a polynucleotide with SEQ ID NO:1 or a polynucleotide encoding a polypeptide with SEQ ID NO:2.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide encoding an amylase with sequence identity as described above because the specification does not establish: (A) a rational and predictable scheme for using all types of complements of SEQ ID NO:1; (B) a rational and predictable scheme for making and using all types of probes of SEQ ID NO:1; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

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Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides having no specific function. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making and using of complements of amylase encoding polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicant has traversed the above rejection arguing that the instant amendments address the enablement issues. While Examiner concurs that the amendment of claims have indeed overcome some enablement issues, it has not addressed the issue of complementary sequences and probes.

### ***Claim Rejections - 35 USC 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-2, 74 and claims 6, 12, 16, 29, 47-48, 74-75, 87-88, 101-106, 130-132 depending therefrom are rejected under 35 U.S.C. 102(b) as being anticipated by Imanaka et al. (GenBank Acc No. E13334, 4-28-1998). This rejection is based upon the public availability of a printed publication. Claims 1, 2 and claim 74 of the instant application are drawn to polynucleotides

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which are complementary to SEQ ID NO:1 and a nucleic acid probe comprising a nucleic acid that specifically hybridizes to SEQ ID NO:1. Imanaka et al. disclose a polynucleotide comprising complementary sequences of SEQ ID NO:1. The very same polynucleotide of Imanaka et al. also comprise sequences having 100% match to portions of SEQ ID NO:1 and therefore can be used as probes. The polynucleotide of Imanaka et al. encode a polypeptide which hydrolyzes starch to glucose. Therefore Imanaka et al. anticipate claims 1, 2, 74 and those depending therefrom as written.

### ***Conclusion***

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'Manjunath N. Rao', with a stylized flourish at the end.

Manjunath N. Rao, Ph.D.  
Primary Examiner  
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April 19, 2006